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Central Nervous System Granulocytic Sarcoma in a Patient With Essential Thrombocythemia

Mario Grande
Second Institute of Medical Clinics, University of Bari, Bari, Italy

We report a rare case of central nervous system granulocytic sarcoma (GS) in a patient with essential thrombocythemia (ET). The diagnosis of GS was established by morphological and cytochemical findings (peroxidase and naphthol-AS-D-chloroacetate esterase positivity) of neoplastic cells. GS was detected as an intracranial frontal mass 7 months before the transformation of ET in acute myeloid leukemia and relapsed as two extradural spinal masses during the course of leukemic evolution. © 1996 Wiley-Liss, Inc.

Key words: granulocytic sarcoma, essential thrombocythemia, CNS tumor

INTRODUCTION

Granulocytic sarcoma (GS) is a rare localized proliferation of immature granulocytic cells infiltrating one or more extramedullary sites [1]. This tumor has been described as a complication of acute myeloid leukemia (AML) [2–5] or chronic granulocytic leukemia (CGL) [5–7] or myelofibrosis with myeloid metaplasia [5] or in association with myelodysplastic disorders in blastic transformation [7,8]. However, rare cases of GS with no prior or subsequent bone marrow disease have been described [5,9]. We report the clinical, morphological, and cytochemical features of a case of central nervous system GS in a man with essential thrombocythemia (ET) preceding the development of AML by 7 months. This association, to the best of our knowledge, has not been previously described.

CASE REPORT

A 41-year-old farmer was apparently well until September 1987, when he complained of dysphagia, dysphonia, paresthesias in the right half of his tongue and severe ipsilateral headache. Physical examination revealed moderate hepatosplenomegaly. The hemoglobin (Hb) was 16 g/dl, and the white blood cell (WBC) count was 18 × 10^9/L with 80% neutrophils, 1% eosinophils, 18% lymphocytes, and 1% monocytes. Platelets were 1,200 × 10^9/L. The bone marrow aspirate was hypercellular with normal myeloid and erythroid maturation and numerous megakaryocytes, which were often found in clusters and tended to show many nuclear lobes. Karyotypic analysis of bone marrow cells was normal. The leukocyte alkaline phosphatase score was 189 (n.v. 20–80). Aggregation response of platelets was normal to collagen but was observed to adenosine diphosphate (ADP) only at high concentrations (3 μM) and was absent to epinephrine also at high concentrations (40 μM). Computed tomography (CT) scan revealed a bilateral frontal mass (Fig. 1). The patient underwent removal of an extradural grayish tumor, eroding the frontal bone and infiltrating the superior sagittal sinus. A subdural noninfiltrating nodule was also found. Microscopic examinations of section and imprint smears of tumor and cytochemical results were compatible with GS (Fig. 2). The patient received 30 Gy to the skull and was treated with busulfan, 4 mg/day. After 1 month, the Hb was 12.9 g/dl, WBC count was 6 × 10^9/L, and platelets 400 × 10^9/L. The patient did relatively well for 3 months, when he presented at our institute with pallor, headache, emesis, and dizziness. Laboratory data revealed Hb 7 g/dl, WBC count 1.1 × 10^9/L with 82% myeloblasts. Platelets count was 50 × 10^9/L. The bone marrow aspirate was hypercellular with 97% myeloblasts. Lactate dehydrogenase (LDH) was increased at 560 IU/L (n.v. 80–240). The liver was palpable 4 cm and the spleen 7 cm below the costal margins. CT brain scan and the cerebrospinal fluid (CSF) were normal. The patient was treated with intravenous dauno-

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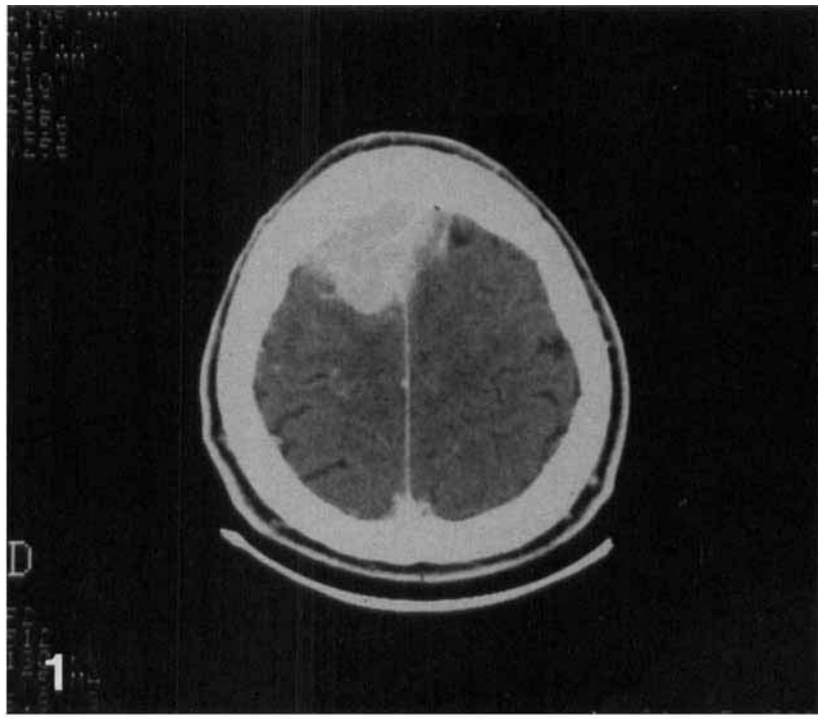
Address reprint requests to Dr. Mario Grande, Via Cavour, 24, 74100 Taranto, Italy.



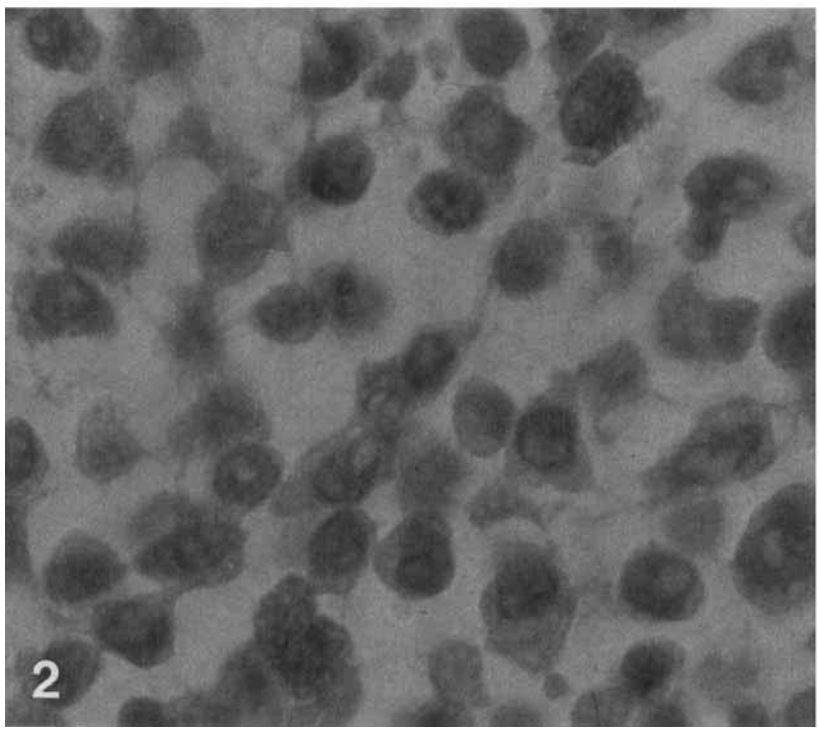


Fig. 1. (Top): CT scan with contrast enhancement reveals an hyperdense frontal mass eroding the frontal bone and invading the superior sagittal sinus.
Fig. 2. (Bottom): Granulocytic sarcoma composed of blast cells with round nuclei and prominent nucleoli. A few eosinophilic cells are present. Hematoxylin & eosin, × 1,000.

rubicin (45 mg/m^2 for 3 days) and cytosine arabinoside (200 mg/m^2 as a continuous infusion daily for 7 days). Three weeks later, the bone marrow was hypercellular, with 2% myeloblasts and normal megakaryocytes. The Hb was 7.2 g/dl, the WBC count 6.1 × 10^9/L with a normal differential, and platelets 336 × 10^9/L. The pa-

tient was given erythrocyte transfusions and received two cycles of consolidation chemotherapy by daunorubicin and cytosine arabinoside. Two months later, the patient developed lumbar pain, CT myelography showed an extradural mass extending from T4 to T6 and spreading to the paravertebral space. The CSF showed 28% myeloblasts, 46% neutrophils, 1% eosinophils, and 25% lymphocytes; Auer rods were seen in some of the blast cells. Hb was 13.6 g/dl, WBC count 7.7 $\times$ 10^9/L, with a normal differential, and platelets were 500 $\times$ 10^9/L. The patient was treated by irradiation with 20 Gy on the thoracic spine, weekly intrathecal injections of cytosine arabinoside (40 mg), and methylprednisolone (30 mg) and intravenous daunorubicin (45 mg/m^2 for 2 days) and cytosine arabinoside (200 mg/m^2 as a continuous infusion daily for 5 days). One month later, the patient presented paresis of the left upper limb. CT myelography showed an extradural tumor at the C4 level invading the left epidural space. The patient was given 12 Gy to the cervical spine. Two weeks later, Hb was 8.4 g/dl, WBC count 6.6 $\times$ 10^9/L with 63% myeloblasts, and platelets were 58 $\times$ 10^9/L. The bone marrow aspirate showed 95.5% myeloblasts. The patient presented with right eyelid ptosis and paresis of the right abducens nerve; he died 6 months after the diagnosis of leukemic transformation of ET was made.

MATERIALS AND METHODS

The peripheral blood smears and the bone marrow aspirate were stained with May–Grünwald-Giemsa. Cytochemical studies were performed on peripheral blood and bone marrow smears by PAS reaction as described by Hayhoe et al. [10], peroxidase as described by Kaplow [11], and naphthol–ASD–chloroacetate esterase as described by Moloney et al. [12]. Sections of intracranial extradural tumor and subdural nodule were stained with hematoxylin and eosin (H&E). Additional sections and imprint smears of intracranial extradural tumor were evaluated with the PAS, peroxidase, and naphthol–ASD–chloroacetate technique.

RESULTS

Microscopic examination of frontal tumor sections disclosed a diffuse infiltration of medium to large blast cells with round to oval nuclei and prominent nucleoli; several eosinophilic myelocytes were present (Fig. 2). Tissue imprints showed a few cytoplasmic azurophilic granules in many of the tumor cells. Blast cells in peripheral blood, bone marrow, CSF smears, and tumor sections and imprint smears were PAS negative and peroxidase and naphthol–ASD–chloroacetate esterase positive.

DISCUSSION

The clinical incidence of GS in AML patient was found to be 2.5–2.9% [6,13]. GS may develop during the course of or as a presenting sign of AML. Neiman et al. [5] reported that 13 of 15 patients with no known disease developed AML within 1–49 months (mean 10 months). Recently, GS was associated with the 8;21 chromosomal translocation in AML [14]. Unfortunately, the karyotype of GS in our case was not determined. Muss and Maloney [6] stated that the incidence of GS is twice as high in patients with CGL that in those with AML. GS was also reported in a few patients with other myeloproliferative disorders as chronic monocytic leukemia, hypereosinophilic syndrome, or myelofibrosis with myeloid metaplasia [5]. GS was never described in patients with ET. Acute leukemic transformation is rare in patients with ET (0.7–3.1%) [15–17], usually of the myeloblastic type [16,18]. Rare cases of acute transformation with lymphoblastic [19] or monocytic [19] or megakaryoblastic [20,21] or basophilic cells [22,23] were observed. In our case of ET, intracranial GS was detected 7 months before the diagnosis of AML was made; other masses were showed in the spinal canal during the course of leukemic transformation of ET. The green color of the neoplasm [24] was absent, but the presence of eosinophilic myelocytes considered highly suggestive of GS [13] was observed.

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